

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C.20231  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 06 June 2000 (06.06.00)
International application No. PCT/EP99/09215
International filing date (day/month/year) 26 November 1999 (26.11.99)
Applicant BEHL, Christian et al

Applicant's or agent's file reference  
19592P WO

Priority date (day/month/year)  
26 November 1998 (26.11.98)

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:  
18 April 2000 (18.04.00)

in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election  was  
 was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Nestor Santesso Telephone No.: (41-22) 338.83.38
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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

## (PCT Article 36 and Rule 70)

Applicant's or agent's file reference 19592P WO	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP99/09215	International filing date (day/month/year) 26/11/1999	Priority date (day/month/year) 26/11/1998	
International Patent Classification (IPC) or national classification and IPC C12N15/12			
Applicant MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG ... et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 18/04/2000	Date of completion of this report 06.02.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Heimann-Pohl, B Telephone No. +49 89 2399 8713



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/09215

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

**Description, pages:**

1-10 as originally filed

**Claims, No.:**

2-21 as originally filed

1 as received on 03/01/2001 with letter of 03/01/2001

**Drawings, sheets:**

1/11-11/11 as originally filed

**Sequence listing part of the description, pages:**

1-23, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/09215

listing has been furnished.

4. The amendments have resulted in the cancellation of:

the description,      pages:  
 the claims,      Nos.:  
 the drawings,      sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):  
*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**II. Priority**

1.  This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:  
 copy of the earlier application whose priority has been claimed.  
 translation of the earlier application whose priority has been claimed.

2.  This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**see separate sheet**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims 1-3
	No:	Claims 4-14
Inventive step (IS)	Yes:	Claims 1,2
	No:	Claims 3, 13-21
Industrial applicability (IA)	Yes:	Claims 1-21
	No:	Claims

2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/09215

1). The present application relates to a human semaphorin, SEMA6A-1, involved in neuronal development and regeneration mechanisms during apoptosis. SEMA6A-1 is capable of a selective binding to members of the Ena/VASP protein family, it contains a cytoplasmic stretch at its C-terminal end sharing homology to Zyxin, a protein known to bind Ena/VASP.

2). Prior Art

D1: DATABASE EMBL - EMROD [Online] Entry/Ac.no. AF030430, 17 November 1997 (1997-11-17) ZHOU, L. ET AL.: 'Mus musculus semaphorin VIa mRNA, complete cds.' XP002134058 -& ZHOU, L. ET AL.: 'Cloning and expression of a novel murine semaphorin with structural similarity to insect semaphorin I' MOLECULAR AND CELLULAR NEUROSCIENCES, US, SAN DIEGO, CA, vol. 9, no. 1, January 1997 (1997-01), pages 26-41, XP002109255

D2: DATABASE EMBL - EMEST8 [Online] Entry/Acc.no. AI249189, 5 November 1998 (1998-11-05) STRAUSBERG, R.: 'qh68h06.x1  
Soares\_fetal\_liver\_spleen\_1NFLS\_S1 Homo sapiens cDNA clone  
IMAGE:1849883 3' similar to TR:O35464 O35464 SEMAPHORIN VIA. ;, mRNA sequence.' XP002134059

D3: DATABASE EMBL - EMEST8 [Online] Entry/Acc.no. AI247563, 5 November 1998 (1998-11-05) STRAUSBERG, R.: 'qh60e03.x1  
Soares\_fetal\_liver\_spleen\_1NFLS\_S1 Homo sapiens cDNA clone  
IMAGE:1849084 3' similar to TR:O35464 O35464 SEMAPHORIN VIA. ;, mRNA sequence.' XP002134060

D4: WO 98 27205 A (GENETICS INST) 25 June 1998 (1998-06-25)

D5: WO 99 32622 A (ZYMOGENETICS INC) 1 July 1999 (1999-07-01)

D6: KOLODKIN ET AL: 'The semaphorin genes encode a family of transmembrane and secreted growth cone guidance molecules' CELL, US, CELL PRESS, CAMBRIDGE, MA, vol. 75, no. 75, 31 December 1993 (1993-12-31), pages 1389-1399-1399, XP002113612 ISSN: 0092- 8674

3). Priority (Box II)

For parts of the present application the priority is not valid. These parts are those which refer to SEMA6A-1 as being capable of a selective binding to members of

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/09215

the Ena/VASP protein family, containing a cytoplasmic stretch at its C-terminal end sharing homology to Zyxin, a protein known to bind Ena/VASP. However, since D5 apparently does not disclose these features, it does not appear to be relevant in this regard.

Furthermore, Fig. 2-8 and examples 1-5 are not contained in the priority document.

4). Novelty and Inventive Step (Box V)

A sequence comparison of SEQ ID NO: 1 with the sequences of D1-D4 revealed the following identities:

D1: 88.9% identity in a 2511 bp overlap

D2: 100.0% identity in a 220 bp overlap

D3: 100.0% identity in a 131 bp overlap

D4: 99.9% identity in a 1730 bp overlap (SEQ ID NO: 7 of D4).

All these sequences hybridize with the sequence SEQ ID NO: 1 of claim 1 under stringent conditions. However, these sequences do not comprise sequences encoding a Zyxin-like domain that binds to the Ena/VASP-like protein as required for the subject matter of claim 1. Thus in view of that essential feature (Zyxin-like domain) claim 1-3 appear to be novel over D1-D4.

However, the modified nucleic acid of claim 4 lacks novelty over D1 and D4 with regard to the section having at least 12 bases from SEQ ID NO: 1 since this section must not contain sequences encoding a Zyxin-like domain. Moreover this feature is not evident in the final product, ie the section having at least 12 bases.

Independent claim 5 does not contain the proviso that a nucleic acid coding for a binding domain of SEMA6A-1 must be present. Thus the sequences of the above cited documents D1-D4 fall under the scope of claim 5 which therefore lacks novelty.

Consequently, also claims 6-12 lack novelty over D1; claims 6-14 lack novelty over D4 (Art. 33 (2) PCT) as far as related to subject matter of claim 4 or 5.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/09215

(Subject matter of claims 6-12 as far as related to claim 1 could be considered as novel)

In view of D1 or D4, which are regarded as the closest prior art documents and, D6 which reports more general on semaphorins, the skilled person had an incentive to look for additional semaphorins in humans bearing in mind the teaching of D6 that this family of transmembrane and secreted proteins are conserved from insects to humans.

However, it cannot be considered as being obviously derivable from these documents that SEQ ID NO: 1 would contain a sequence encoding a Zyxin-like domain that binds to the Ena/VSAP-like protein, which is considered as the inventive and essential feature of semaphorin6A-1. Therefore claim 1 and 2 involve an inventive step (Art. 33 (3) PCT).

Claim 3 is not limited to said functional feature (binds to the Ena/VSAP-like protein) thus it is not clear whether the nucleic acid must encode a functional Zyxin-like domain. Therefore said claimed nucleic acid lacks an inventive step.

With regard to the reasons for lack of novelty for claims 4 and 5 the thereon depending claims 13-21 cannot be called inventive in view of D1 or D4 alone or in combination with D6 (see above)(Art. 33 (3) PCT).

PCT/EP99/09215  
Max-Planck-Gesellschaft...  
19592P WO

03. Jan. 2001

**New Claim**

1. Nucleic acid coding for human semaphorin 6A-1 comprising:
  - (a) the nucleotide sequence shown in SEQ ID NO:1,
  - (b) a sequence corresponding to the nucleotide sequence shown in SEQ ID NO:1 within the degeneration of the genetic code,  
or
  - (c) a sequence which hybridizes with the sequences of (a) or/and (b) under stringent conditions

with the proviso that it contains a nucleic acid coding for a binding domain of human semaphorin 6A-1 comprising:

  - (d) the nucleotide sequence shown in SEQ ID NO:3,
  - (e) a sequence corresponding to the nucleotide sequence shown in SEQ ID NO:3 within the degeneration of the genetic code,  
or
  - (f) a sequence which hybridizes with the sequences of (d) or/and (e) under stringent conditions.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>19592P WO</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 99/09215</b>	International filing date (day/month/year) <b>26/11/1999</b>	(Earliest) Priority Date (day/month/year) <b>26/11/1998</b>
Applicant <b>MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG .. ET AL</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.  
 It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the language, the International search was carried out on the basis of the International application in the language in which it was filed, unless otherwise indicated under this item.
  - the International search was carried out on the basis of a translation of the International application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the International application, the International search was carried out on the basis of the sequence listing :
  - contained in the International application in written form.
  - filed together with the International application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the International application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).3.  Unity of invention is lacking (see Box II).

## 4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

**HUMAN SEMAPHORIN GA-1 (SEMAGA-A), A GENE INVOLVED IN NEURONAL DEVELOPMENT AND REGENERATION MECHANISMS DURING ADOPTOSIS, AND ITS USE AS A POTENTIAL DRUG TARGET**

## 5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International search report, submit comments to this Authority.

## 6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

8 None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

EP 99/09215

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C12N15/62 C07K16/18 A61K38/17  
 G01N33/53 C12Q1/68 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL - EMROD 'Online!    Entry/Ac.no. AF030430,    17 November 1997 (1997-11-17)    ZHOU, L. ET AL.: "Mus musculus semaphorin    VIA mRNA, complete cds."    XP002134058</p> <p>the whole document    -&amp; ZHOU, L. ET AL.: "Cloning and    expression of a novel murine semaphorin    with structural similarity to insect    semaphorin I"    MOLECULAR AND CELLULAR    NEUROSCIENCES, US, SAN DIEGO, CA,    vol. 9, no. 1, January 1997 (1997-01),    pages 26-41, XP002109255</p> <p>the whole document</p> <p>---</p> <p>-/-</p>	1-12
Y		13-21



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## ° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the International search

Date of mailing of the International search report

27 March 2000

10/04/2000

## Name and mailing address of the ISA

European Patent Office, P.B. 5018 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Smalt, R

## INTERNATIONAL SEARCH REPORT

International Application No

EP 99/09215

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 11216 A (KIKUCHI KAORU ;KIMURA TORU (JP); SUMITOMO PHARMA (JP)) 19 March 1998 (1998-03-19) whole document, particularly the claims. & EP 0 960 937 A the whole document ----	13-21
X	WO 98 27205 A (GENETICS INST) 25 June 1998 (1998-06-25) page 21, line 19 -page 22, line 9 seq.ID's 7 and 8. ----	1-14
Y	DATABASE EMBL - EMEST8 'Online! Entry/Acc.no. AI249189, 5 November 1998 (1998-11-05) STRAUSBERG, R.: "qh68h06.x1 Soares_fetal_liver_spleen_1NFLS_S1 Homo sapiens cDNA clone IMAGE:1849883 3' similar to TR:035464 035464 SEMAPHORIN VIA. ;, mRNA sequence." XP002134059 the whole document ----	1-14
Y	KOLODKIN ET AL: "The semaphorin genes encode a family of transmembrane and secreted growth cone guidance molecules" CELL, US, CELL PRESS, CAMBRIDGE, MA, vol. 75, no. 75, 31 December 1993 (1993-12-31), pages 1389-1399-1399, XP002113612 ISSN: 0092-8674 the whole document ----	1-14
A	DATABASE EMBL - EMEST8 'Online! Entry/Acc.no. AI247563, 5 November 1998 (1998-11-05) STRAUSBERG, R.: "qh60e03.x1 Soares_fetal_liver_spleen_1NFLS_S1 Homo sapiens cDNA clone IMAGE:1849084 3' similar to TR:035464 035464 SEMAPHORIN VIA. ;, mRNA sequence." XP002134060 the whole document ----	19, 21
A	HALL, K.T. ET AL.: "Human CD100, a novel leukocyte semaphorin that promotes B-cell aggregation and differentiation." PROC.NAT'L.ACAD.SCI.USA, vol. 93, October 1996 (1996-10), pages 11780-5, XP002134057 abstract ----	19, 21
A	WO 95 07706 A (UNIV CALIFORNIA) 23 March 1995 (1995-03-23) whole document, particularly the claims. ----	1-4, 8, 10

**INTERNATIONAL SEARCH REPORT**

International Application No

EP 99/09215

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 99 32622 A (ZYMOGENETICS INC) 1 July 1999 (1999-07-01) the claims page 3, line 22 - line 24; figure 2 seq.ID's 1 and 2 page 12, line 24 -page 13, line 34 -----	1-16,18

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/EP 99/09215

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 9811216	A 19-03-1998	AU EP	4136797 A 0960937 A	02-04-1998 01-12-1999
WO 9827205	A 25-06-1998	AU EP	5706198 A 0958360 A	15-07-1998 24-11-1999
WO 9507706	A 23-03-1995	US AU AU CA EP JP US US US	5639856 A 683494 B 7724094 A 2171638 A 0721342 A 9505725 T 5935865 A 6013781 A 5807826 A	17-06-1997 13-11-1997 03-04-1995 23-03-1995 17-07-1996 10-06-1997 10-08-1999 11-01-2000 15-09-1998
WO 9932622	A 01-07-1999	AU	2000299 A	12-07-1999